



# **Armed Forces College of Medicine AFCM**



# **Gastric secretion**

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# INTENDED LEARNING OBJECTIVES (ILO)



By the end of this session, the student will be able to:

- Describe the composition of gastric secretion and the function of each constituent.
- Describe mechanism of HCl formation.
- Mention stimuli of HCl secretion.
- Describe the different mechanisms that regulate gastric secretions.
- Explain causes and consequences of disturbed HCl secretion.

# Lecture Plan



1. Part 1 (5 min) Introduction
2. Part 2 (35 min) Main lecture
3. Part 3 (5 min) Summary
4. Lecture Quiz (5 min)

# Gastric Secretion



- Gastric glands secrete about **2.5 litres/day** of acidic( pH 1) juice which is composed of:

**Electrolytes:  $H^+$ ,  $Cl$ ,  $Na^+$  and  $K^+$**

**Enzymes: Pepsin, gelatinase, lipase**

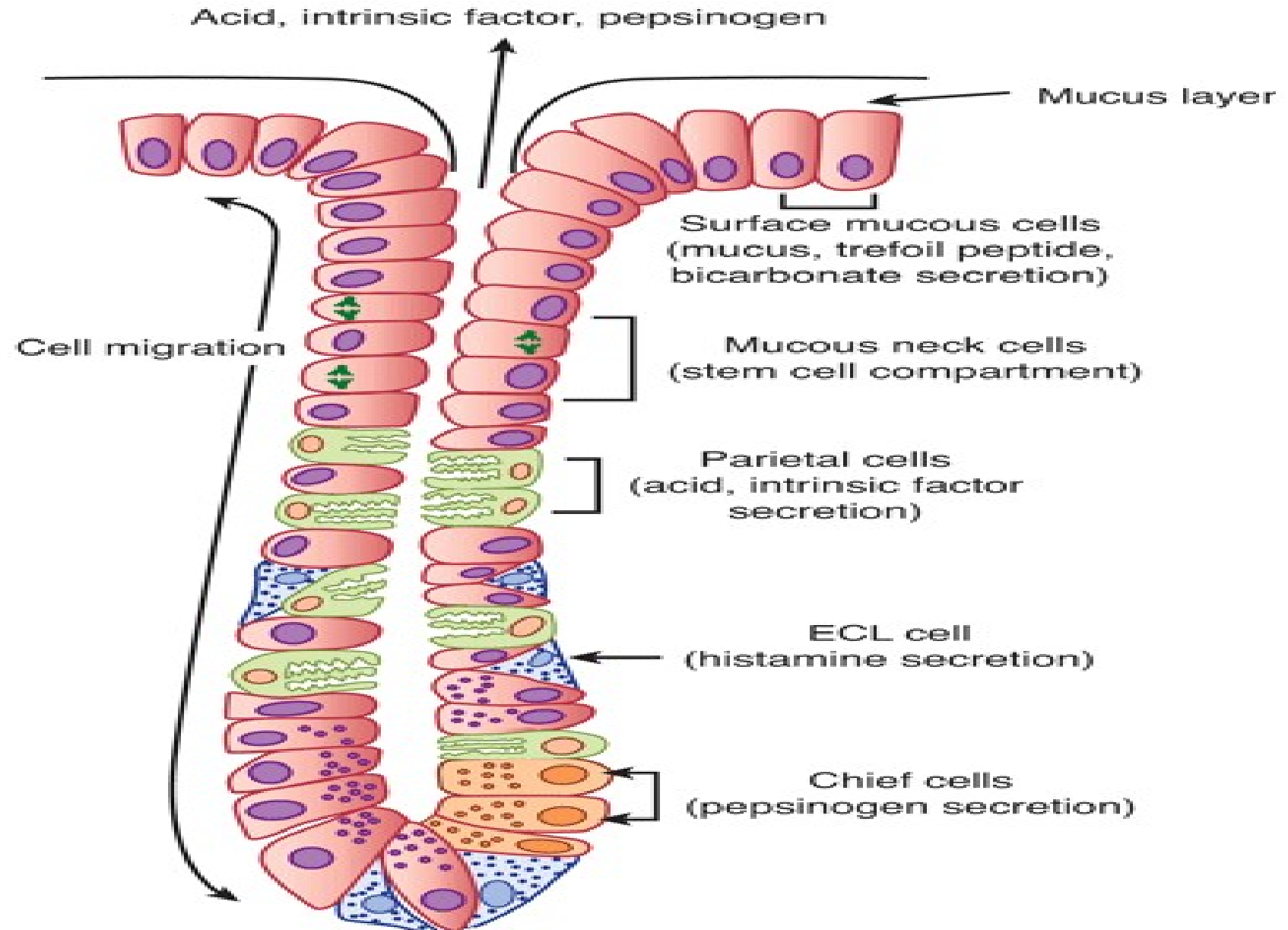
**Mucus**

**Intrinsic factor**

**Water**



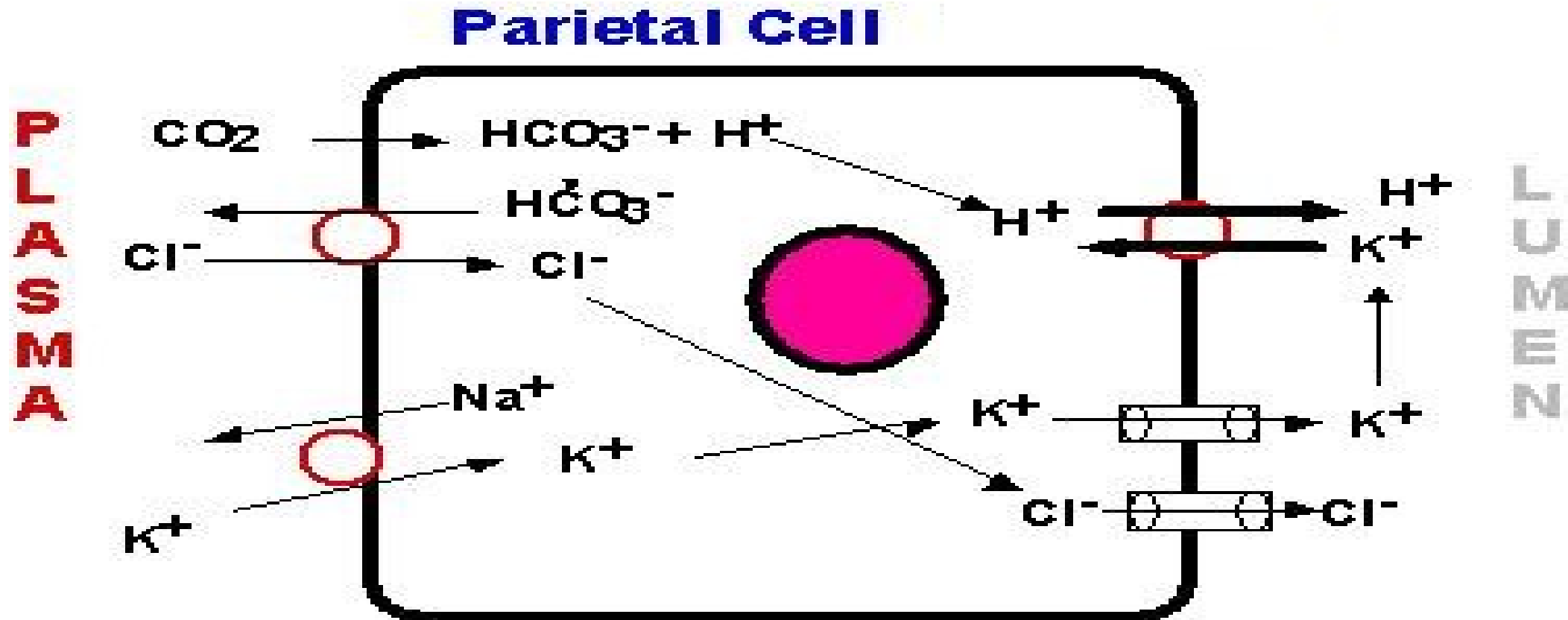
# Gastric Glands



# Acid Secretion



- An active process.
- Secreted by the parietal cells.



## Mechanism of Acid Secretion



- $\text{H}^+ - \text{K}^+$  ATPase in the apical membrane of the parietal cells pumps  $\text{H}^+$  out of the cells in exchange to  $\text{K}^+$ . This occurs against the concentration gradients, and need energy, provided by hydrolysis of ATP.
- $\text{H}_2\text{CO}_3$  is formed by the hydration of  $\text{CO}_2$  by carbonic anhydrase in the parietal cells.



## Mechanism of Acid Secretion



- $\text{H}^+$  is pumped into lumen, while  $\text{HCO}_3^-$  is extruded by an antiport in the basal membrane of the parietal cells that exchanges  $\text{Cl}^-$ .
- $\text{Cl}^-$  is extruded down its electro-chemical gradient through channels.
- pH of systemic blood rises and the urine becomes alkaline during  $\text{HCl}$  s. This is called "Post prandial alkaline tide".



# Mechanism of Acid Secretion



## Alkaline Tide

As HCl is secreted by the parietal cells  $\text{HCO}_3^-$  is added to the gastric venous blood so the PH of the blood increases.





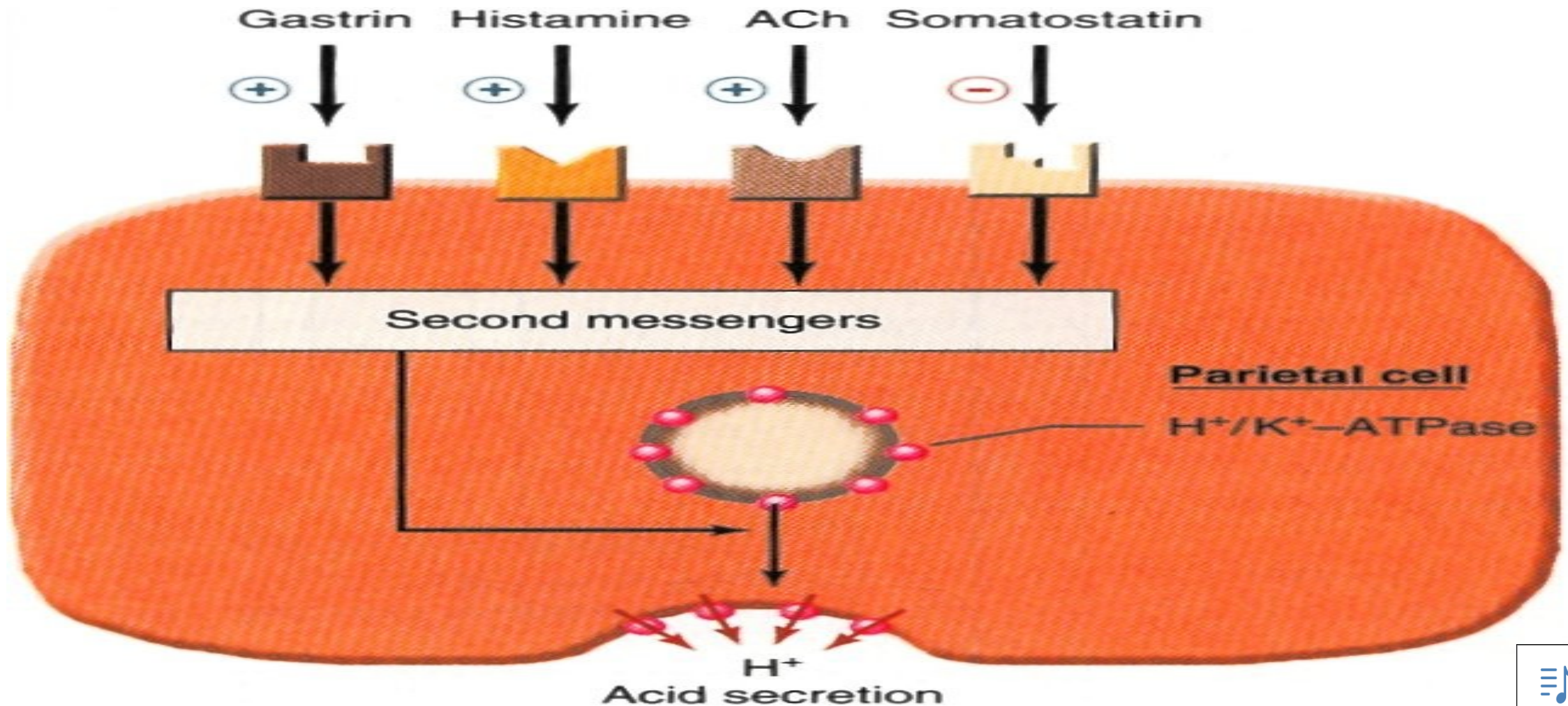
# Stimuli of HCl Secretion



- **Histamine from enterochromafen cells:** acts via  $H_2$  receptors.  $H_2$  receptor stimulation increases intracellular cAMP.
- **Acetylcholine from vagal nerve endings:** acts via  $M_3$  muscarinic receptors.
- $M_3$  receptor stimulation increases intracellular  $Ca^{++}$ .
- **Gastrin from G cells:** it acts either directly on oxyntic cells by increasing intracellular  $Ca^{++}$  (like acetylcholine) or indirectly through stimulating the secretion of histamine from enterochromaffin-like cells (ECL cells).



# Stimuli of HCl Secretion



# Functions of HCl



- **Maintains relative sterility of the stomach by killing ingested bacteria.**
- **Dissolves food particles and changes food into "chyme".**
- **Activates the inactive pepsinogen into active pepsin.**
- **Provides optimum pH for the action of pepsin.**
- **Helps iron and calcium absorption.**
- **Stimulates the flow of bile.**



## Secretion and activation of pepsinogen



- The pepsinogen secreted by chief (peptic) cells, is activated by HCl at pH 2 to active pepsin. This active pepsin further activates pepsinogen i.e. **positive feedback mechanism**. Pepsin digests proteins into peptones and peptides. Pepsin is inactivated by the alkalinity of the duodenum.



## Secretion of intrinsic factor



- Secreted by the parietal cells along with the hydrochloric acid.
- Absorption of B<sub>12</sub>.



# When parietal cells are stimulated, they secrete:

- (a) HCl and intrinsic factor.
- (b) HCl and pepsinogen
- (c) HCl and HCO<sub>3</sub><sup>-</sup>
- (d) HCO<sub>3</sub><sup>-</sup> and HCO<sub>3</sub><sup>-</sup>
- (e) mucus and pepsinogen

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(e) mucus and pepsinogen

# Secretion of mucus in the stomach



- ***There are two types of mucus:***

## **Soluble mucus:**

It is secreted by mucous neck cells of the gastric glands in response to vagal stimulation. It lubricates the gastric chyme.

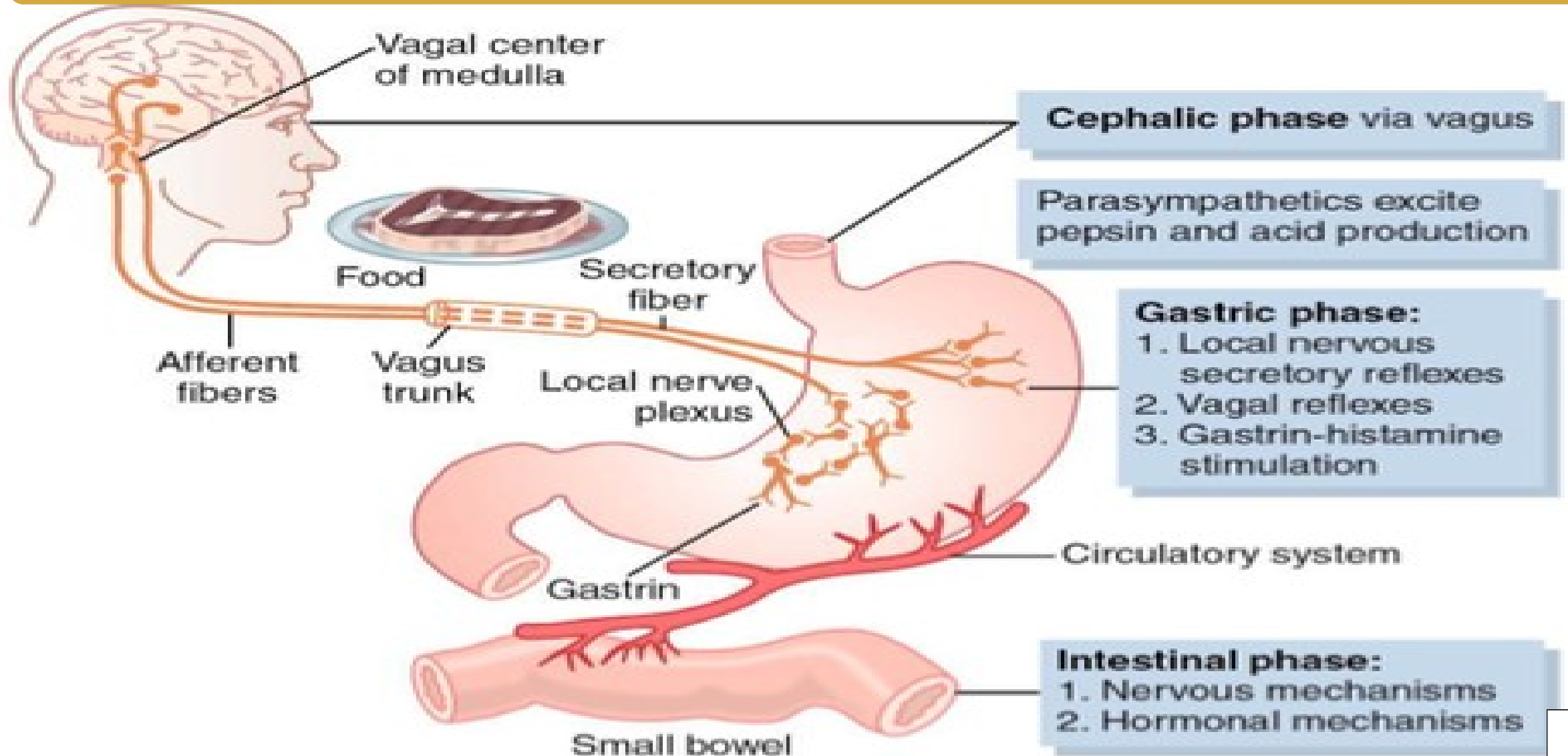
## **Insoluble mucus:**

It is secreted by the surface epithelium of the gastric body and fundus, as well as esophageal and pyloric junctions. It forms a layer 1.5mm in thickness, to protect the gastric mucosa against the mechanical friction with food, and to neutralize the corrosive effect of the acid.





# Phases of gastric secretion



# Control of gastric secretion



Gastric secretion occurs in three phases: a cephalic phase, a gastric phase and an intestinal phase.

## **(I) The cephalic stimulatory phase: (Nervous)**

- Conditioned and unconditioned reflexes stimulate the dorsal nucleus of the vagus to increase secretions of HCl, pepsinogen, mucus and gastrin.
- Accounts for about one third of the gastric secretion.
- The efferent fibres for this reflex are in the vagus nerves.



## Control of gastric secretion



### - Vagal stimulation increases gastric secretion by:

- **Acetylcholine** which acts directly on the cells in the glands in the body and fundus.
- **Gastrin:** vagal nerve endings release gastrin-releasing peptide that increases gastrin secretion.



# Control of gastric secretion



## (II) The gastric stimulatory phase: (Nervous and Hormonal):

This phase accounts for **2/3** of the total gastric secretion.

### **mechanisms:**

Food in the stomach.

1- Long vagovagal reflexes like in cephalic phase.

2- Local enteric reflexes. Receptors in the wall of the stomach and the mucosa respond to stretch and chemical stimuli (mainly amino acids and related products of digestion). The sensory fibres from the receptors enter the submucous plexus then **they synapse on postganglionic parasympathetic neurons** (enteric nervous system) that end on parietal cells and stimulate acid secretion.

trin secretion.



# Control of gastric secretion



## **(III) The intestinal inhibitory phase: (Nervous and Hormonal):**

- Presence of food in the duodenum.
- Depression of gastric secretion by:

### **1- Enterogastric reflex:**

Enterogastric reflex which occurs as a result of increased acid, fat content, hypertonic solutions, hypotonic solutions or distension of duodenum.



## Mechanisms of inhibition of gastric secretion



2- Hormones which inhibit gastric secretion, such as GIF, VIP, CCK and secretin.

Somatostatin hormone which acts by a **paracrine manner**:

Direct action: inhibit parietal cells directly.

Indirect action: inhibit histamine release from enterochromaffin cells.

3- Emotional depression and fear, via impulses from cerebral cortex, inhibit the dorsal vagal nucleus.



# Mucosal barrier



**he barrier is formed of:**

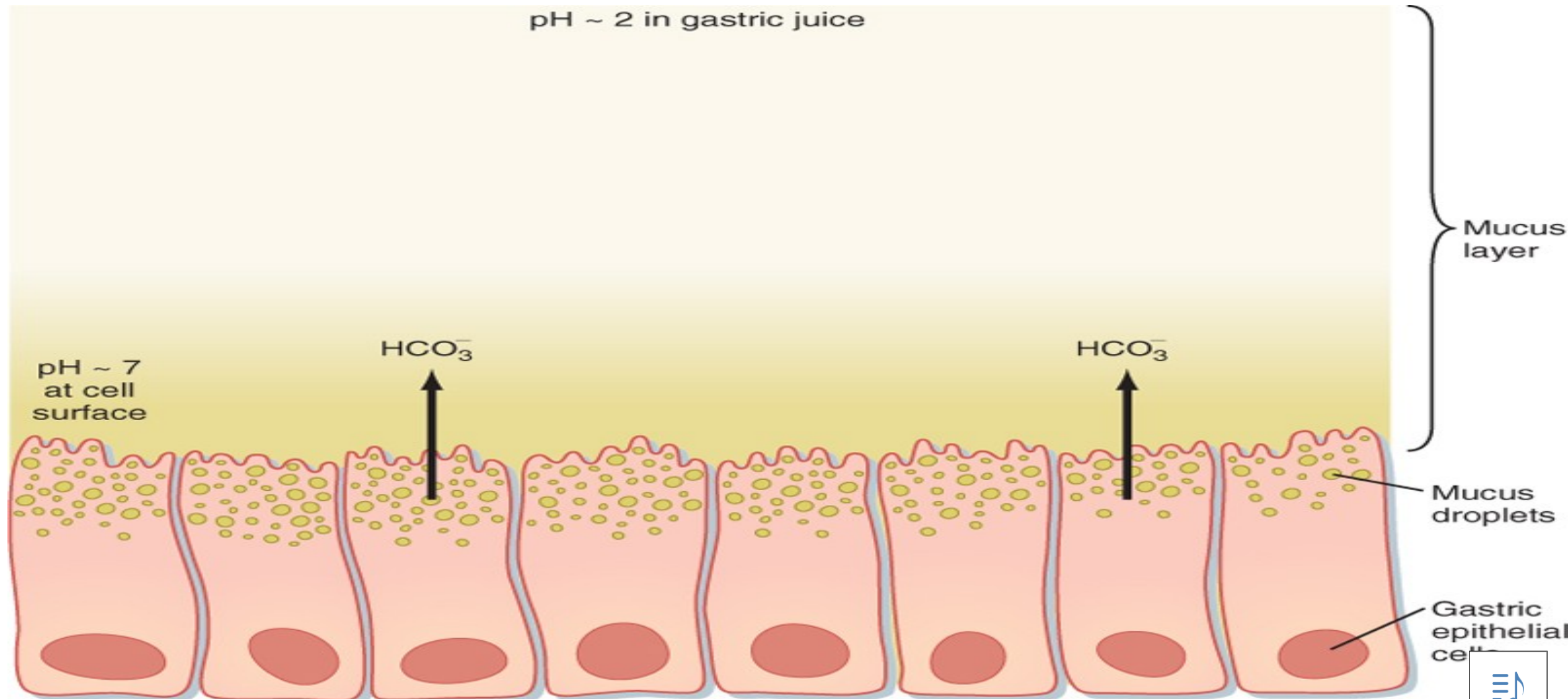
**The insoluble mucus, which forms a gel like layer covering the mucous membrane.**

**The integrity of the membrane of the mucosal cells: The membrane is impermeable to hydrogen ions**

**an active transport mechanism pumping  $H^+$  ions from the mucosal cell into the gastric lumen.**



# Mucosal barrier





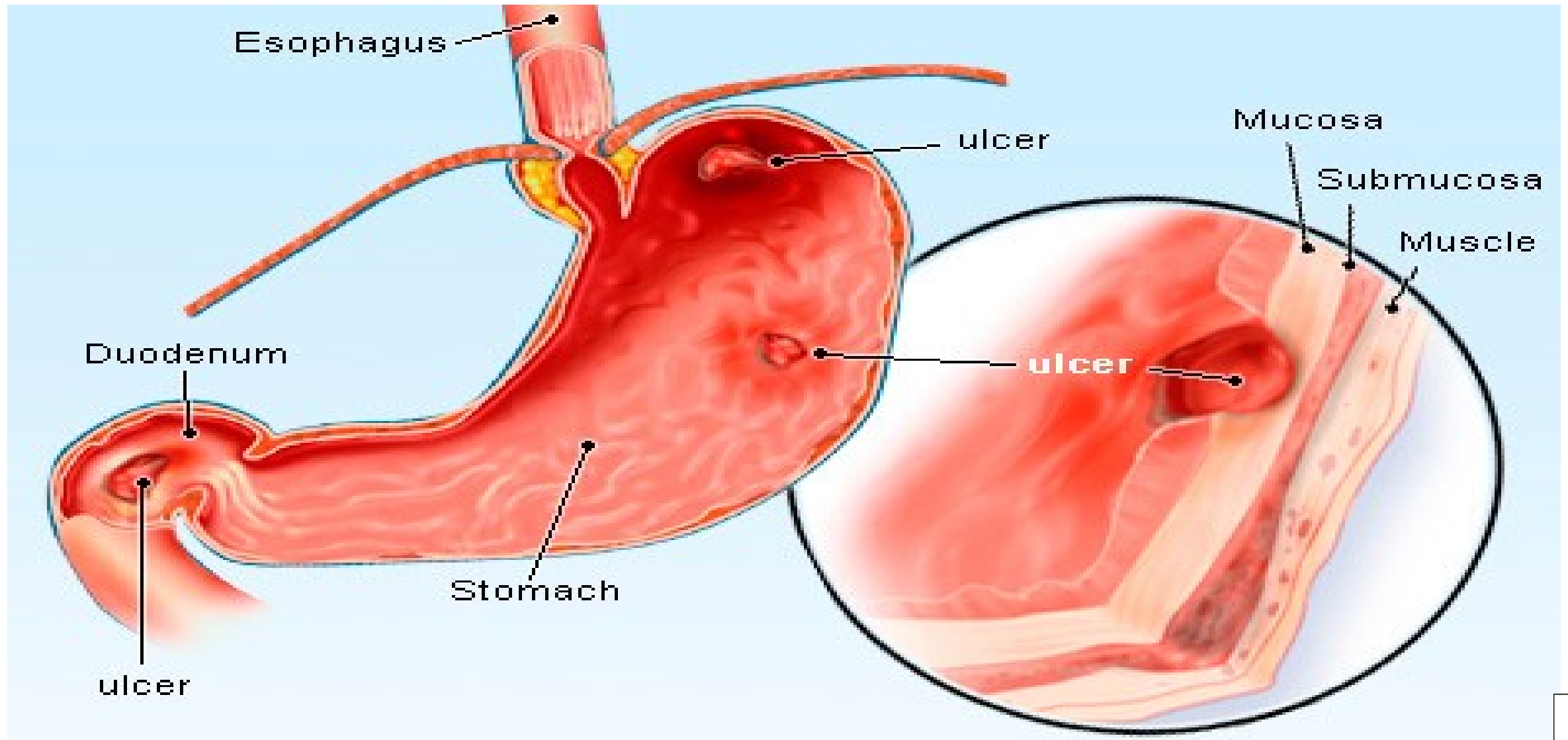
## Mucosal barrier



- **Prostaglandins** stimulate mucus and bicarbonate secretion.
- inhibit acid secretion.
- increase mucosal blood flow.



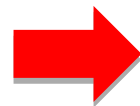
# Peptic ulcer



# Peptic ulcer



## Causes of peptic ulcers:



### 1) Breakdown of the gastric mucosal barrier :

**Alcohol**

**Asprin**, and non-steroidal anti- inflammatory drugs; both inhibit the production of prostaglandins and consequently decrease mucus and  $\text{HCO}_3^-$  secretion.

**Infection** with specific bacteria called *Helicobacter pylori* which disrupts the mucosal barrier.



# Peptic ulcer



**Causes of peptic ulcers:**

**2-Excess secretion of HCl:**



Zollinger-Ellison syndrome, there is excess secretion of gastrin hormone by tumors in the pancreas. Gastrin causes prolonged secretion of acid and severe ulcers.



# Treatment of Peptic ulcer



- Inhibition of acid secretion:
  - Blockage of  $H_2$  histamine receptors on the parietal cells, e.g. by cimetidine.
  - Inhibit  $H^+-K^+$  ATPase in the apical membrane of parietal cells by proton pump inhibitors e.g. **Omeprazole**.
- Eradication of *Helicobacter pylori* with antibiotics.
- Stop use of aspirin and non-steroidal anti-inflammatory drugs.
- Surgical removal of gastrin-secreting tumors.

## Summary



The parietal cells secrete HCl into the lumen of the stomach and concurrently add  $\text{HCO}_3^-$  into the blood stream.

Stimuli of HCl secretion include acetylcholine, gastrin and histamine.

$\text{H}_2$  receptor blocking drugs such as cimetidine inhibit  $\text{H}^+$  secretion by blocking the stimulatory effect of histamine.

Histamine potentiates the action of Ach and gastrin in stimulating HCl secretion.





## Question 1

**Which of the following is secreted by stimulation of the parietal cell?**

- a) HCl and intrinsic factor.
- b) HCl and pepsinogen.
- c) HCl and  $\text{HCO}_3^-$ .
- d)  $\text{HCO}_3^-$  and intrinsic factor.
- e) Mucus and pepsinogen.





## Question 2

**A patient with duodenal ulcer is treated with cimetidine, a drug that inhibits  $H^+$  secretion by parietal cells. Which of the following is the mechanism of cimetidine action?**

- a) Block muscarinic receptors.
- b) Stimulation of muscarinic receptors.
- c) Blocks  $H-K^+$  ATPase.
- d) Decreased level of cAMP.
- e) Inhibition of somatostatin.





## Question 3

**A 44-year old woman is diagnosed with Zollinger-Ellison syndrome. Which of the following findings is consistent with the diagnosis?**

- a) Decreased serum gastrin levels.
- b) Increased insulin serum level.
- c) Decreased parietal cell mass.
- d) Peptic ulcer disease.
- e) Increased absorption of dietary lipids.



## SUGGESTED TEXTBOOKS



1. Guton and Hall 11<sup>th</sup> edition, from page 795 to 799.
2. Ganong's 25<sup>th</sup> edition, from page 457 to 460.
3. Linda & Costanza 6<sup>th</sup> edition, from page 360 to 366.



**Thank you**